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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/534,626	05/11/2005	Toren Finkel	4239-67020-02	8541

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EXAMINER	
KAUSHAL, SUMESH	
ART UNIT	**PAPER NUMBER**
1633	

MAIL DATE	DELIVERY MODE
12/24/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/534,626	FINKEL ET AL.	
	Examiner	Art Unit	
	Sumesh Kaushal	1633	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *02 August 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-16, 20-29 and 48-59* is/are pending in the application.

4a) Of the above claim(s) *20-29 and 51-53* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-16, 48-50 and 54-59* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 09/02/08 has been entered.

Claims 1-16, 20-29 and 48-59 are pending and are examined in this office action.

This application contains claims 20-29 and 51-53 are drawn to an invention nonelected with traverse in the reply filed on 08/14/07. A complete reply to the final rejection must include cancellation of nonelected claims or other appropriate action (37 CFR 1.144) See MPEP § 821.01.

Note: Earlier applicant elected Group I claims 1-16 and 48-50. Therefore, claims 1-16, 48-50 and 54-59 are examined in this office action, whereas claims 20-29 and 51-53 that represented Group III stand withdrawn from further consideration.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-16, 48-50 and 54-59 are rejected under 35 U.S.C. 103(a) as being unpatentable over Vasa et al[A] (Circ. Res. 89(1):E1-7, 2001, ref. of record on PTO-1449), Vasa et al[B] (Circulation. 103(24):2885-90, 2001, ref. of record on PTO-1449) and Scott et al (Circulation. 104:491-496, 2001).

The instant claims are drawn to a method of diagnosing decreased or increased vascular function in a subject by enumerating endothelial progenitor cells in a blood sample from a subject. In addition the claims are further drawn to a method of diagnosing increased vascular function in a subject by enumerating endothelial progenitor cells in a blood sample from a subject in response to a cholesterol-lowering agent.

Vasa et al[A] teaches number and migratory activity of circulating Endothelial Progenitor Cells (EPCs) inversely correlate with risk factors for coronary artery disease (CAD). The cited art further teaches enumeration of EPCs in CAD patients and normal controls. The cited art teaches the isolation and enumeration of EPCs from the peripheral blood of patients with coronary artery disease (CAD) and compared the results to a control sample (see abstract, page 4, fig(s) 2-4). The cited art teaches that mononuclear cells were isolated by density-gradient centrifugation of peripheral blood (page 2, co.1 para.4). The cited art teaches that circulating EPCs are considered to be characterized by expression of CD34 and the VEGF receptor KDR. The cited art further teaches enumeration of CD34/KDR(VEGFR2^{+}) double-positive EPCs, which inherently express CD31(DAKO) (see Vasa page 1, col.1, page 6, col.1 para 2, also see *Asahara et al Science ;275:964–967, 1997, ref of record on PTO1449*). The cited art further teaches that CD34-/KDR-positive cells were significantly reduced by ≈48% in patients with CAD compared with 9 age-matched healthy volunteers (see Fig 4A). The cited art concluded that the number of risk factors was inversely correlated with the levels of CD34-/KDR-positive cells (page 3. col.2 para.2). The cited art further teaches that increased age and elevated LDL cholesterol serum levels significantly correlated with lower numbers of CD34-/KDR-positive cells (Fig 4D and 4E). The cited art further teaches that that several experimental studies indicate a significant contribution of EPCs for adult neovascularization, the reduction in the number of EPCs and their functional impairment might contribute to reduced vascularization in patients with CAD. The cited art further teaches that age (senescence), hypertension, smoking, cholesterol levels, and a positive family of CAD, as well as the overall number of risk factors, have all been shown to be associated with impaired endothelium-mediated vasodilator function of the

coronary circulation. Therefore, one may speculate that the impairment of circulating EPCs may contribute to an insufficient regeneration of the endothelium, which may lead to endothelial dysfunction (page 6, col.1 para 1, table-1).

Vasa et al[B] teaches increase in circulating EPCs by statin therapy in patients with stable coronary artery disease (CAD). The cited art teaches enumeration of EPCs in patients treated with blood cholesterol lowering agent atorvastatin (page 2888 fig-3, fig-4). The cited art demonstrated that statin therapy is associated with an increase in the number of circulating EPCs in patients with stable CAD. The cited art teaches the isolation and enumeration of EPCs from the peripheral blood of patients with coronary artery disease (CAD) and compared the results to a control sample (see page 2887, fig-2A). The cited art further teaches enumeration of EPCs expressing CD34+/KDR (VEGFR2^{+}) which inherently express CD31(DAKO) (see Vasa page 2887 col.2 para. 2, page 2888, col.1; also see Asahara et al *Science* ;275:964–967, 1997). The cited art further teaches that the results of the present study demonstrate that statin therapy is associated with an increase in the number of circulating EPCs in patients with stable CAD. The increased number of EPCs was paralleled by an enhancement of the migratory capacity of isolated EPCs. Mobilization of circulating EPCs with enhanced functional activity might contribute to the well-established beneficial effects of statins in patients with CAD as it is well established that EPCs participate in repair after ischemic injury (page 2889, col.1 para. 2). The cited art further teaches that statin therapy has shown to rapidly enhance coronary blood flow in patients with stable CAD and to reduce myocardial ischemia after an acute ischemic episode within a few weeks of treatment (page 2889, col.2 para. 4).

Even though Vasa et al[A] and Vasa et al[B] teach the enumeration of endothelial progenitor cells for the diagnosis of increase or decrease of vascular function using baseline clinical characteristics similar to Framingham Risk Score factors encompassing variety of cardio vascular disease parameters (i.e. hypertension, diabetes, smoking, family history of CAD, lipid profiles etc) the Vasa et al [(AB)] do not specifically teaches the use of Framingham Risk Score.

Scott et al' report was derived from a workshop on cardiovascular risk assessment sponsored by the National Heart, Lung, and Blood Institute, which addressed whether risk equations developed in the Framingham Heart Study (FHS) for predicting new-onset coronary heart disease (CHD) apply to diverse population groups. Preparation for the workshop included a reanalysis and comparison of prospective studies in several different populations in which risk factors were related to cardiovascular outcomes. The report further states that that the population baseline risk of Native Americans likewise was similar to the FHS population. For other populations (PRHS and HHS), calibration adjustments to the FHS equations improved their performance greatly. The report concluded that for each specific cohort, the use of study-specific risk equations improved the ability to predict CHD morbidity and mortality compared with FHS equations, even if only slightly.

Thus it would have been obvious to one ordinary skilled in the art at the time the instant invention was made to modify the invention of Vasa et al[A] and Vasa et al[B] with Scott et al to include Framingham Risk Score factors equations. One would have been motivated to do so to because Framingham Risk Score has been historically used to in the variety of cardiovascular studies. One would have a reasonable expectation of success, since the use of Framingham Risk Score equations has been routine in the art at time the instant invention was made. Thus all of the claimed elements were known in the prior art, and one skilled in the art could have combined the elements as claimed by known methods with no change in their respective functions, and the combination would have yielded predictable result to one of ordinary skill in the art at the time of the invention (*See KSR International Co. v. Teleflex Inc.*, 82 USPQ2d 1385, U.S. 2007). Given the teachings of the prior art and the level of skill of the ordinary skilled artisan at the time the instant invention was made, it must be considered that said ordinary skilled artisan would have had reasonable expectation of success in practicing the claimed invention. Therefore the invention as claimed is prima facie obvious in view of cited prior art of record.

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sumesh Kaushal whose telephone number is 571-272-0769. The examiner can normally be reached on Mon-Fri. from 9AM-5PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joseph Woitach can be reached on 571-272-0739. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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